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(54) **METHOD FOR PREPARATION OF PHARMACEUTICAL PRODUCTS**

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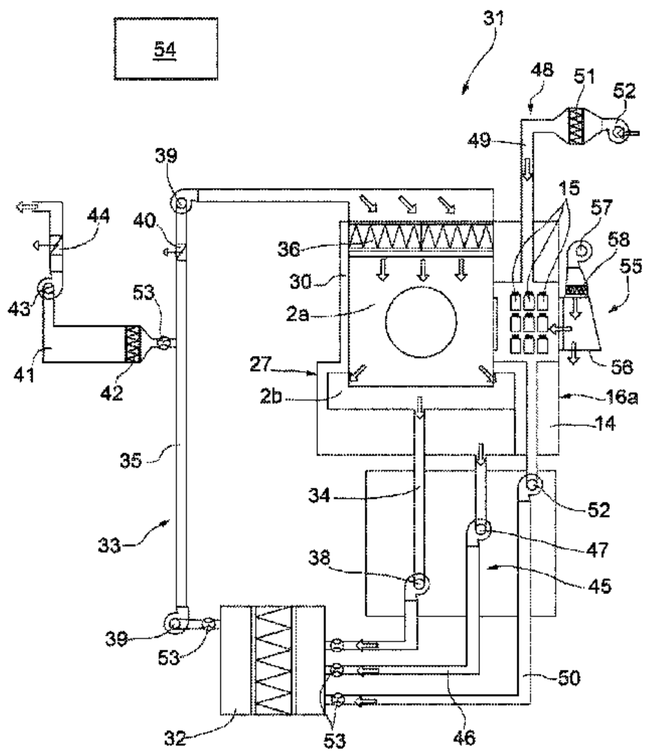
(57) **ABSTRACT**

A method for the preparation of pharmaceutical products is provided that utilizes a machine having a containing liner, a dosing chamber for preparing at least one pharmaceutical product accommodated within the containing liner, and a pneumatic ventilation device for feeding two air flows through the dosing chamber and through the containing liner, respectively. Operation of the pneumatic ventilation device is selectively controlled so that the containing liner has inside a pressure lower than a pressure existing within the dosing chamber and than a pressure existing in the environment outside the containing liner itself.

12 Claims, 5 Drawing Sheets



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B08B 15/02	(2006.01)
F24F 3/16	(2006.01)
B01F 15/02	(2006.01)

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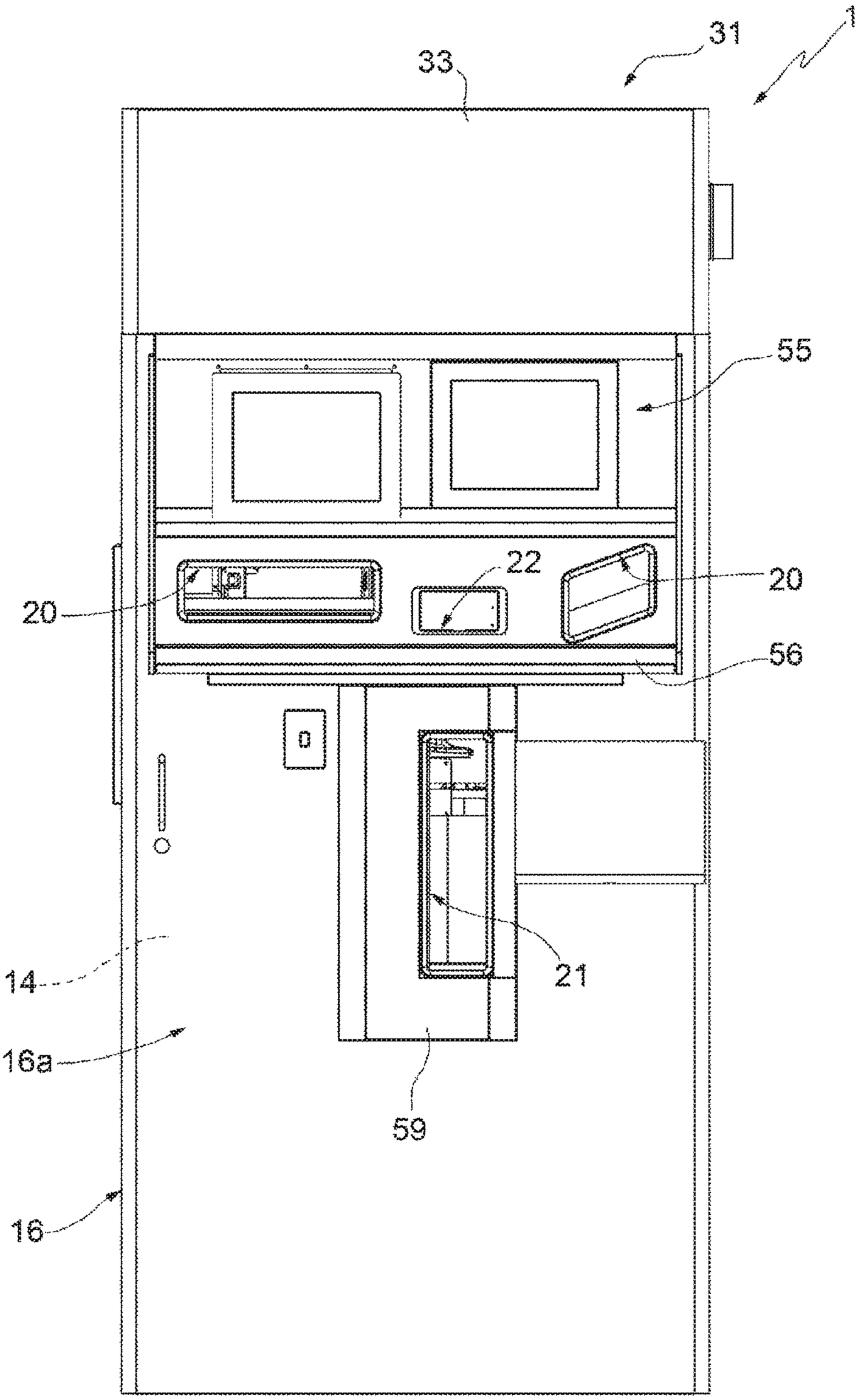

FIG.1

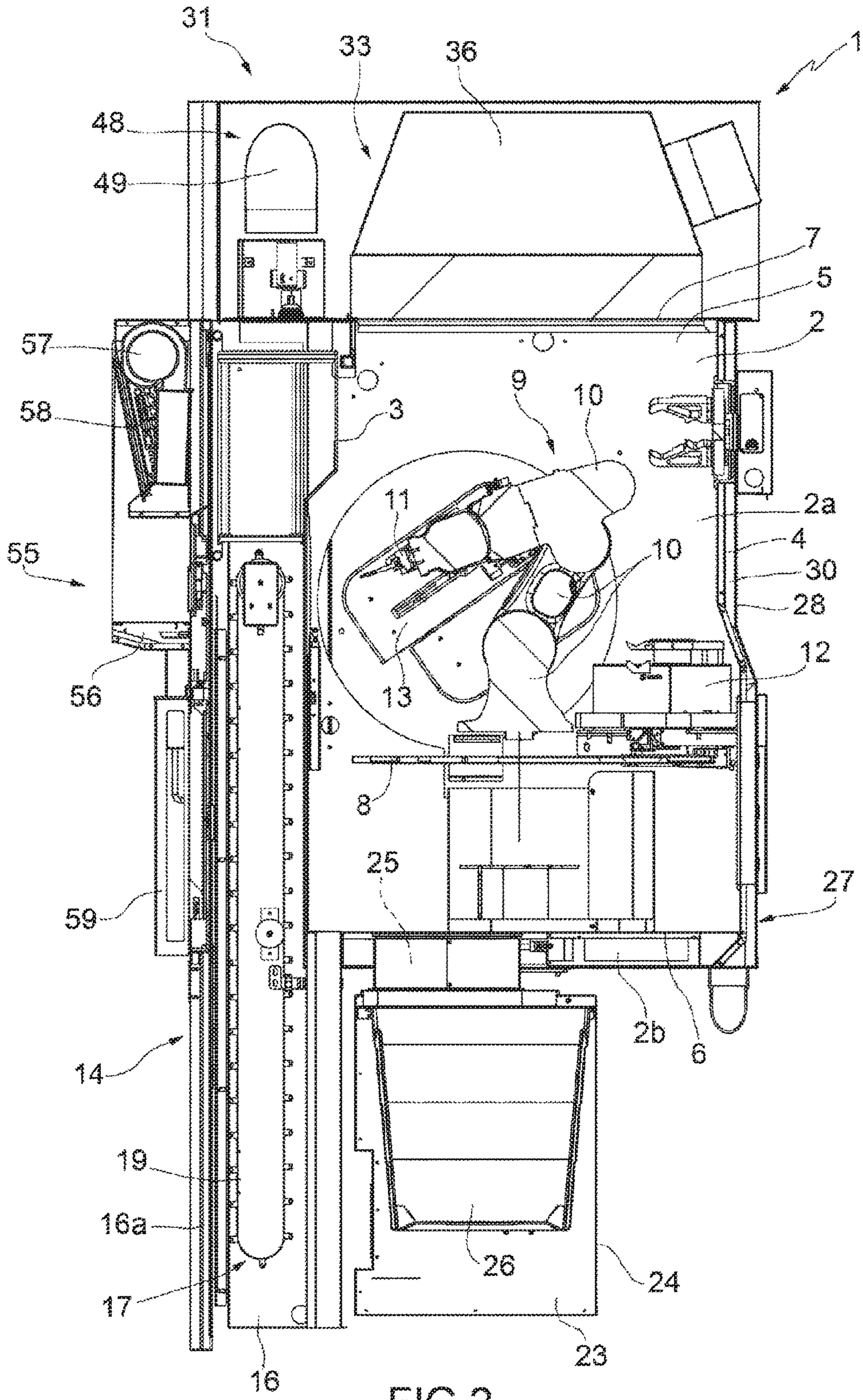
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FIG.2

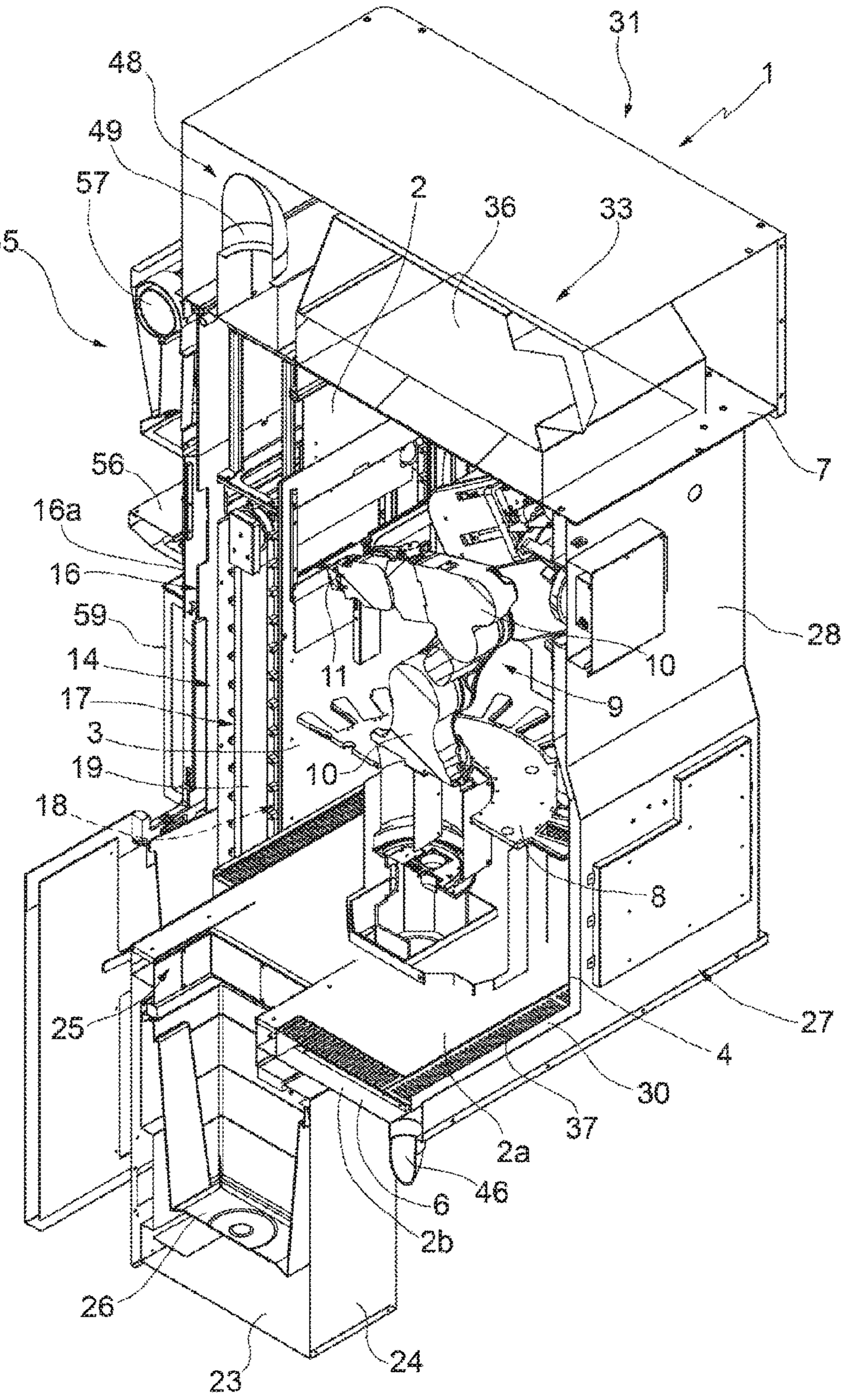
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FIG.3

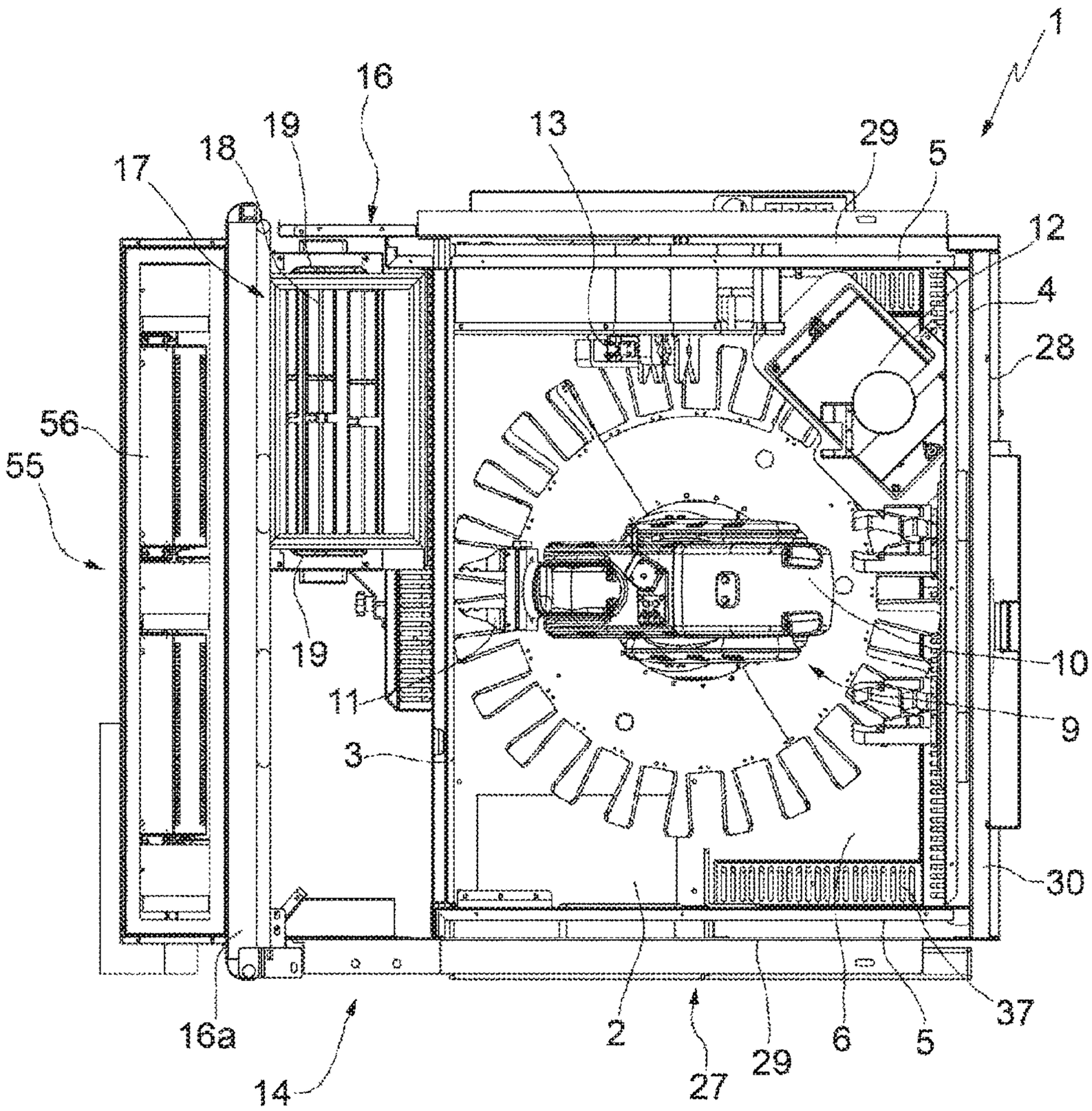

FIG.4

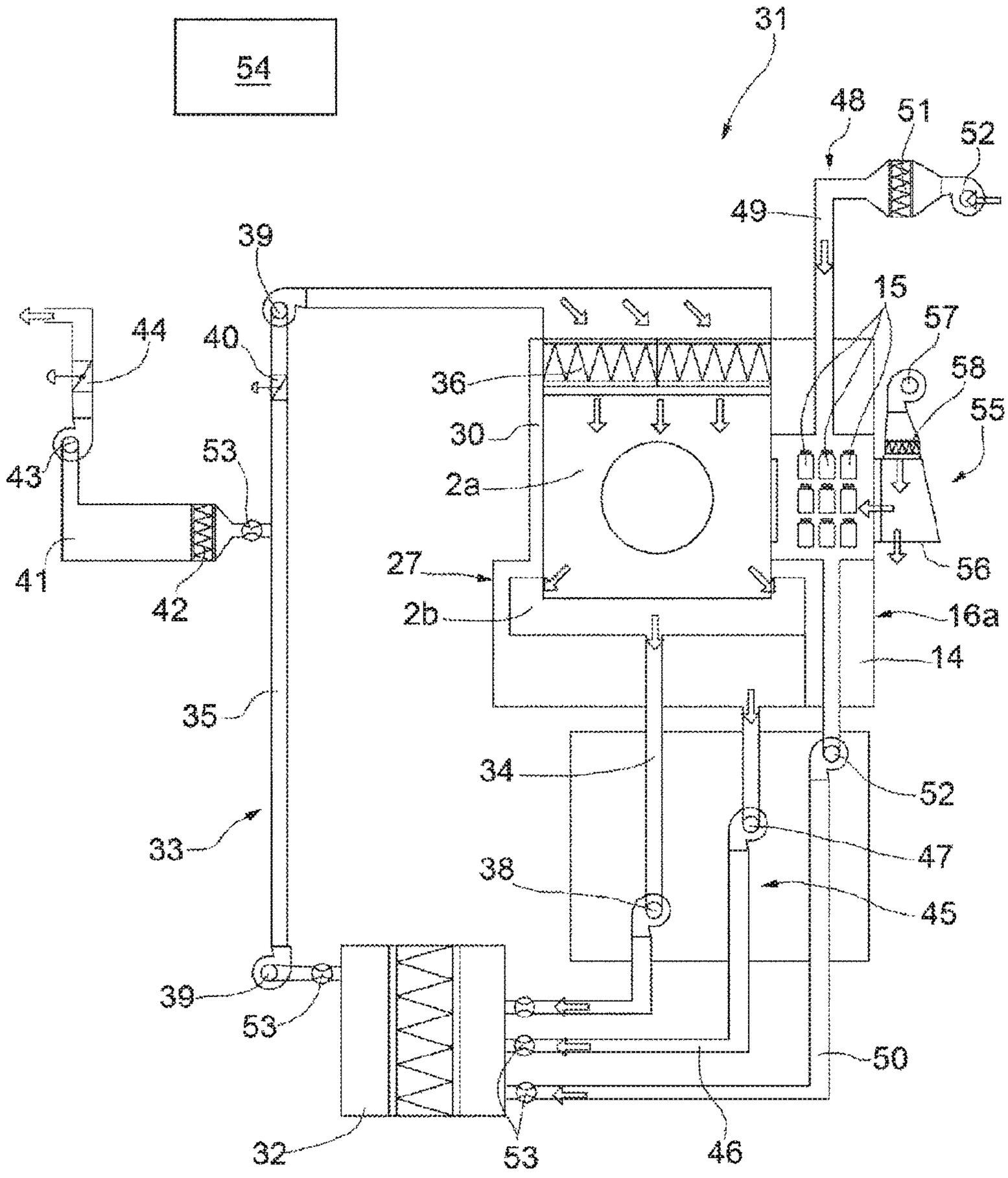
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FIG.5

METHOD FOR PREPARATION OF PHARMACEUTICAL PRODUCTS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation patent application that claims priority benefit to a co-pending non-provisional patent application entitled "Machine for the Preparation of Pharmaceutical Products," which was filed on Jun. 5, 2014, and assigned Ser. No. 14/362,980, which in turn claims the benefit of PCT/IB2012/056998, which was filed on Dec. 5, 2012, which in turn claims the benefit of European Application No. 11192020.3, which was filed on Dec. 5, 2011, all of which are herein incorporated by reference in their entireties.

TECHNICAL FIELD

The present invention relates to a machine for the preparation of pharmaceutical products.

BACKGROUND ART

A machine is known in the field of the preparation of pharmaceutical products, in particular of the preparation of toxic pharmaceutical products, such as, for example, cytostatic drugs used for chemotherapy, comprising a store for a plurality of containers, e.g. infusion bags, bottles and syringes; a dosing station for the preparation of a pharmaceutical product obtained by mixing, by means of a syringe, at least one pharmaceutical substance contained in a bottle and at least one diluent contained in an infusion bag; a weighing station of the containers; and a robotized arm for gripping and transporting the containers themselves.

The store, the dosing station, the weighing station and the robotized arm are accommodated within a containment chamber limited by a protective casing provided with an access opening adapted to allow personnel to load and/or unload the various types of containers into/from the store itself.

In order to protect the health of personnel and to avoid the diffusion of toxic substances outside the containing chamber, the machine normally comprises a pneumatic ventilation device for feeding an air flow through the containing chamber itself.

The pneumatic ventilation device is selectively controlled so that the pressure existing in the containing chamber is lower than the pressure existing in the environment outside the containing chamber itself.

The known machines for the preparation of pharmaceutical products of the type described above have some drawbacks mainly deriving from the fact that the various pressures existing in the containing chamber and in the environment outside the containing chamber prevent the diffusion of toxic substances from the containing chamber into the outside environment, but do not prevent the diffusion of contaminating agents from the outside environment into the containing chamber.

DISCLOSURE OF INVENTION

It is an object of the present invention to provide a machine for the preparation of pharmaceutical products which is free from the above-described drawbacks, and which can be simply and cost-effectively implemented.

According to the present invention, a machine for the preparation of pharmaceutical products is provided as claimed in the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described with reference to the accompanying drawings, which show a non-limitative embodiment thereof, in which:

FIG. **1** is a diagrammatic front view, with parts removed for clarity, of a preferred embodiment of the machine according to the present invention;

FIG. **2** is a diagrammatic side view, with parts in section and parts removed for clarity, of the machine in FIG. **1**;

FIG. **3** is a diagrammatic perspective view, with parts in section and parts removed for clarity, of the machine in FIG. **1**;

FIG. **4** is a diagrammatic plan view, with parts in section and parts removed for clarity, of the machine in FIG. **1**; and

FIG. **5** diagrammatically shows the operation of a pneumatic ventilation device fitted in the machine in FIG. **1**.

BEST MODE FOR CARRYING OUT THE INVENTION

With reference to FIGS. **1**, **2**, **3** and **4**, reference numeral **1** indicates as a whole a machine for the preparation of pharmaceutical products comprising a dosing chamber **2** limited, in the case in point, by a front wall **3** and by a rear wall **4**, substantially vertical and parallel to each other, by two substantially vertical side walls **5**, perpendicular to the walls **3** and **4**, by a substantially horizontal bottom wall **6**, and by a substantially horizontal upper wall **7**, parallel to the wall **6** itself.

Chamber **2** accommodates therein a pocket drum **8** for storing infusion bags (not shown); a robotized gripping and transporting device **9**, which is fitted in the drum **8**, comprises a plurality of articulated arms **10** hinged to each other, and is provided with a gripping member **11** fitted on the free end of the arms **10**; a weighing device **12** of the infusion bags (not shown); and a dosing station **13** for the preparation of a pharmaceutical product.

Furthermore, the machine **1** has a store **14**, which allows the storage of a plurality of containers **15** (in the case in point, bottles and syringes which can also be weighed on the device **12**), and comprises a parallelepiped-shaped box-like body **16** coupled to the front wall **3** so as to protrude downwards from chamber **2**.

Store **14** accommodates therein two pocket conveyor devices **17** (only one of which is shown in FIGS. **2** and **3**), each of which is shaped to store a given type of container **15**, and has a plurality of pockets **18** fitted between a pair of belt conveyors **19**.

The containers **15** of each device **17** are loaded into and/or taken from the respective pocket **18** through a first opening **20** obtained through a front wall **16***a* of body **16** and normally closed by a first access door (not shown) and through a second opening (not shown) obtained through the wall **3** and normally closed by a second access door (not shown).

The mentioned infusion bags (not shown) are transferred to and from the drum **8** by means of a linear conveyor (known and not shown), which is engaged in sliding manner by an adapter member fitted on each infusion bag (not shown), communicates with the environment outside the machine **1** through an opening **21** obtained through the wall **16***a* and normally closed by an access door (not shown), and

further communicates with chamber **2** through an opening (not shown) obtained through the wall **3** and normally closed by an access door (not shown).

Furthermore, store **14** comprises a vibration distribution plate (not shown) for a plurality of closing caps (not shown) of the mentioned syringes (not shown).

The vibrating distribution plate (not shown) is accommodated within body **16**, is loaded by the personnel with closing caps (not shown) through an opening **22** obtained through the wall **16***a* and normally closed by an access door (not shown), and communicates with chamber **2** by means of an opening (not shown) obtained through the wall **3** and normally closed by an access door (not shown).

Furthermore, the machine **1** comprises a chamber **23** for collecting the machining waste of the machine **1** itself.

Chamber **23** is obtained under chamber **2**, is limited by a box-like body **24** fitted under the wall **6**, and communicates with chamber **2** through an opening **25** obtained through the wall **6** and normally closed by an access door (not shown).

Chamber **23** accommodates therein a container **26** for collecting the machining waste of the machine **1** adapted to be extracted from chamber **23** through a hatch (not shown) defining part of the body **24** after having been closed and sealed automatically with a lid (not shown) within chamber **23** itself.

Store **14** and therefore body **16** jointly define with chamber **23**, and thus with the body **24**, part of a containing liner **27** of chamber **2**.

The liner **27** further comprises a rear wall **28** substantially superimposed on the wall **4** and two side walls **29** substantially superimposed on walls **5**.

The walls **4**, **28** and the walls **5**, **29** mutually define a gap **30** closed at the bottom by wall **6** and at the top by wall **7**.

The machine **1** is provided with a pneumatic ventilation device **31** comprising a main filtering unit **32** and a first feeding circuit **33** for feeding an air flow through chamber **2**.

Circuit **33** comprises an inlet branch **34** for feeding the air from chamber **2** into the unit **32**, and an outlet branch **35** for feeding the air from the unit **32** firstly through a secondary filtering unit **36** fitted over the wall **7**, and thus into chamber **2**.

In this regard, it is worth noting that the bottom wall **6** of chamber **2** is shaped as a double wall adapted to divide chamber **2** itself into an upper chamber **2***a* and a lower chamber **2***b* connected to each other by means of a peripheral intake grille **37** which facilitates the direction of the air flow from chamber **2***a* to chamber **2***b*.

Circuit **33** is further provided with a variable flow rate impeller **38** arranged along the branch **34**, two adjustable flow rate impellers **39** arranged along the branch **35**, and an on-off valve **40** arranged along the branch **35** between the two impellers **39**.

The device **31** further comprises a discharge pipe **41** of at least part of the air from the unit **32** into the outside environment.

The pipe **41** is connected to the branch **35** between the two impellers **39** and upstream of the valve **40** in a direction of advancement of the air along the branch **35**, and has a filtering unit **42**, an adjustable flow rate impeller **43**, and a flow rate adjustment valve **44** arranged in sequence and in order along the pipe **41** itself.

The device **31** further comprises a second feeding circuit **45** for aspirating an air flow from chamber **23** and from gap **30**.

Circuit **45** comprises an inlet branch **46** for feeding air from liner **27** into unit **32**, and an adjustable flow rate impeller **47** fitted along the branch itself **46**.

Furthermore, the device **31** has a feeding circuit **48** for feeding an air flow through store **14** and thus body **16**.

The circuit **48** comprises an inlet branch **49** for feeding air from the outside environment into body **16**, an outlet branch **50** for feeding air from body **16** into the unit **32**, a filtering unit **51** fitted along the branch **49**, and two adjustable flow rate impellers **52** fitted along branch **49** and branch **50**, respectively.

Furthermore, each branch **34**, **35**, **46**, **50** is provided, similarly as, the pipe **41**, with a device **53** for measuring the air flow rate fed along the branch **34**, **35**, **46**, **50** or along the pipe **41**.

The operation of the impellers **38**, **39**, **47**, **52**, and thus the air flow feed through chamber **2** and store **14** and the air flow aspirated through the gap **30**, are selectively controlled by means of an electronic control unit **54** as a function of the signals coming from the devices **53** and by further measuring devices (not shown) of the pressures existing within chamber **2**, store **14**, gap **30**, and the outside environment so that the pressure within the liner **27** is lower than the pressure within chamber **2** and the pressure in the outside environment and the pressure in chamber **2** is higher than the pressure in the outside environment.

In other words, the pressure within the liner **27** on one hand allows the possible diffusion of toxic substances from chamber **2** into liner **27** but prevents the diffusion thereof from liner **27** into the outside environment, and on the other hand allows the possible diffusion of contaminants from the outside environment into liner **27** but prevents the possible diffusion from liner **27** into chamber **2**.

From the above, it derives that the toxic substances present inside chamber **2** cannot jeopardize the health of personnel and that the contaminants present in the outside environment cannot compromise the correct preparation of the pharmaceutical products in chamber **2** itself.

When the front wall **3** of chamber **2** is opened to allow cleaning and/or maintenance operations of chamber **2** itself, the on-off valve **40** fitted along the branch **35** is closed, and the impeller **43** is activated to discharge the air fed along branch **35** into the outside environment and make the pressure in chamber **2** substantially equal to the pressure in liner **27** and lower than the pressure in the outside environment.

When one of the access doors (not shown) obtained through front wall **3** of chamber **2** is opened to allow the robotized device **9** to load/unload containers **15** or the mentioned closing caps (not shown) of the syringes to/from store **14**, the pressure in chamber **2**, being higher than the pressure in body **16**, diverts part of the air flow fed along the branch **35** from chamber **2** into body **16** itself. As the mentioned access doors are mainly arranged at an upper zone of chamber **2**, the air diverted from chamber **2** into body **16** thus comes from the filtering unit **36** without coming into contact with the possible contamination zones.

When the access door (not shown) obtained through the front wall **3** of chamber **2** is opened to allow the introduction/removal of the infusion bags into/from chamber **2**, the pressure in chamber **2**, being higher than the pressure in body **16**, diverts part of the air flow fed through chamber **2** in body **16** itself. As the mentioned access door (not shown) is arranged at a lower zone of chamber **2** and between the two conveyor devices **17** of containers **15**, the air diverted

from chamber **2** in body **16** is thus immediately taken from branch **50** of the feeding circuit **48** without coming into contact with containers **15**.

When one of the access doors (not shown) obtained in the wall **16***a* is opened to load/unload containers **15** or the mentioned infusion bags (not shown) or the mentioned closing caps (not shown) of the syringes into/from store **14**, the entrance of contaminants present in the outside environment into store **14** is obstructed by a feeding flow **55**, which feeds an air flow along the wall **16***a*, and defines part of the device **31**.

Circuit **55** comprises a shelf **56** fitted underneath the openings **20** and **22**, and an adjustable flow rate impeller **57** fitted over the openings **20** and **22** for feeding an air flow taken from the outside environment firstly through a filtering unit **58** and thus to shelf **56**.

The air flow generated by the impeller **57** is fed to shelf **56** in substantially vertical direction, and thus taken in by a frame **59** fitted about opening **21**, diverted by frame **59** in substantially horizontal direction, fed on opening **21**, and finally discharged downwards again into the outside environment.

As the pressure in body **16** is lower than the pressure in the environment outside the machine **1**, the air flow fed along the wall **16***a* defines, on one hand, an air barrier adapted to obstruct the introduction of contaminants inside store **14**, and on the other is diverted in part inside store **14** through the access door (not shown) opened each time.

Consequently, the activation of circuit **55** obstructs the introduction of air coming from the outside environment into body **16** allowing the introduction into body **16** of filtered air coming from unit **58**.

According to some variants (not shown):

feeding circuit **45** is eliminated and replaced with a feeding circuit similar to circuit **33** and adapted to feed an air flow through the gap **30**;

containing liner **27** is shaped so as to fully envelop dosing chamber **2** at the front wall **3**, the rear wall **4** and the side walls **5**, both at the bottom wall **6** and the upper wall **7**.

The invention claimed is:

1. A method for preparation of pharmaceutical products, the method comprising:

a) providing a machine (**1**) for preparing at least one pharmaceutical product via at least one dosing chamber (**2**) provided with a mixing assembly (**13**) and a pneumatic ventilation device (**31**), wherein the machine (**1**) further comprises a containing liner (**27**) that extends about the dosing chamber (**2**) so as to define a first containing chamber (**23**, **30**) and a second containing chamber (**16**) for a store (**14**) for a plurality of containers (**15**) containing at least one of pharmaceutical product and diluents therein;

b) generating air flow via the pneumatic ventilation device (**31**), wherein a first air flow is directed into the dosing chamber (**2**) and at least one second air flow is directed into the containing liner (**27**);

c) selectively controlling the pneumatic ventilation device (**31**) with a control unit (**54**), wherein said control unit (**54**) controls the pneumatic ventilation device (**31**) so as to control the first and second air flows, so that the containing liner (**27**) has inside a pressure lower than a pressure existing within the dosing chamber (**2**) and a pressure lower than a pressure existing in the environment outside the containing liner (**27**) itself;

d) feeding the first air flow through the dosing chamber (**2**) via a first feeding circuit (**33**);

e) aspirating the second air flow from the first containing chamber (**23**, **30**) via a second feeding circuit (**45**);

f) feeding a third air flow through the second containing chamber (**16**) via a third feeding circuit (**48**);

g) providing a loading station (**56**) of the containers (**15**) into the store (**14**) and at least one communication door for connecting the store (**14**) and the environment outside the containing liner (**27**) to each other; and

h) feeding a fourth air flow from the pneumatic ventilation device (**31**) along and external to said at least one communication door via a fourth feeding circuit (**55**), wherein said fourth air flow is external to the containing liner (**27**) and obstructs introduction of air from the environment outside the containing liner (**27**).

2. The method as recited in claim **1**, wherein the control unit (**54**) is effective to control the pressure existing in the dosing chamber (**2**) at a higher level than the pressure existing in the environment outside the containing liner (**27**).

3. The method as recited in claim **1**, wherein the pneumatic ventilation device (**31**) further comprises, for each said feeding circuits (**33**, **45**, **48**), at least one respective impeller (**38**, **39**, **47**, **52**) for feeding the respective air flow along the feeding circuit (**33**, **45**, **48**) itself.

4. The method as recited in claim **3**, wherein for each said impeller (**38**, **39**, **47**, **52**), a respective adjustment valve (**44**) for selectively controlling the air flow fed by the impeller (**38**, **39**, **47**, **52**) itself along the respective feeding circuit (**33**, **45**, **48**).

5. The method as recited in claim **1**, wherein said control unit (**54**) measures the air flow fed along the feeding circuit (**33**, **45**, **48**) itself.

6. The method as recited in claim **1**, wherein the pneumatic ventilation device (**31**) further comprises a first filtering unit (**32**); each of said feeding circuits (**33**, **45**, **48**) comprising an inlet branch (**34**, **46**, **50**) of the respective air flow in the first filtering unit (**32**).

7. The method as recited in claim **6**, wherein the first feeding circuit (**33**) further comprises an outlet branch (**35**) of the respective air flow from the first filtering unit (**32**); the pneumatic ventilation device (**31**) further comprising a second filtering unit (**36**) arranged along the outlet branch (**35**) itself.

8. The method as recited in claim **7**, wherein the outlet branch (**35**) is connected to the dosing chamber (**2**) for feeding air coming from the first filtering unit (**32**) to the dosing chamber (**2**), is further connected to the discharge pipe (**41**) for discharging at least part of the air coming from the first filtering unit (**32**) into the external environment, and is provided with an on-off valve (**40**) fitted along the outlet branch (**35**) downstream of the discharge pipe (**41**).

9. The method as recited in claim **8**, wherein the pneumatic ventilation device (**31**) comprises a third filtering unit (**42**) arranged along said discharge pipe (**41**).

10. The method as recited in claim **1**, wherein said control unit (**54**) measures the pressure in the dosing chamber (**2**), the pressure in the containing liner (**27**) and the pressure in the outside environment.

11. The method as recited in claim **1**, wherein the pressure within the containing liner (**27**) allows for the possible diffusion of substances from dosing chamber (**2**) into containing liner (**27**) but prevents the diffusion thereof from containing liner (**27**) into the outside environment.

12. The method as recited in claim **1**, wherein the pressure within containing liner (**27**) allows for the possible diffusion of substances from the outside environment into containing

liner (**27**) but prevents the possible diffusion from containing liner (**27**) into dosing chamber (**2**).

* * * * *